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IMPLEMENTATION OF BIOFEEDBACK IN CLOSED  
LOOP OF HEART RATE VARIABILITY AND PACED  
BREATHING IN PATIENTS WITH ARTERIAL  
HYPERTENSION IN REAL CLINICAL PRACTICE

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# Introduction

- **Arterial hypertension (AH) is a serious, debilitating disease, that is not only medical but also social and economic problem worldwide:**
  - **about 45% of adults aged from 25 years old have high blood pressure,**
  - **74.3% are aware about the disease,**
  - **just 43% are treated,**
  - **efficacy of the treatment is only 13%.**
- **Maintaining achieved target blood pressure (BP) levels in patients with AH continues to represent an urgent problem.**
- **Key point of AH is an imbalance of regulatory systems.**
- **Low efficiency of pharmacotherapy boosted searching for non-drug methods.**
- **Promising tool of adjunctive therapy in patients with AH can be biofeedback (BFB) in the closed loop of paced breathing under the control of heart rate variability (HRV) parameters.**

# Introduction

- **Biofeedback** is the process of gaining greater awareness of many physiological functions primarily using instruments that provide information on the activity of those same systems, with a goal of being able to manipulate them at will.
- **HRV** is one of the first systems that responds to subtle environmental influences, which makes it a convenient loop of biofeedback.
- **Paced breathing** is a method of influence on the state of the regulatory systems of the body
  - **comfortable:** easy to implement (patient need to breathe with a certain specified frequency);
  - **flexible:** at the respective frequencies it can selectively affect specific links of the HRV spectrum.

## Objective

- The purpose of the research is to study the effectiveness of biofeedback in a closed loop of heart rate variability and paced breathing in patients with arterial hypertension in real clinical practice.

# Our patients



**Patient 1: male, 64 y/o, retired, lives in the city, admitted to the hospital in November 2014.**



**Patient 2: male, 60 y/o, retired, lives in the city, admitted to the hospital in October 2014.**

*Permission to publish photos of patients was obtained.*

# Complaints on admittance

periodical increase of BP up to 150/100 mm Hg, usually in the morning, followed by headache in occipital area and/or dizziness.

episodic increase of BP up to 150/90 mm Hg, usually in the morning, which followed by headache in frontal and temporal areas.

## Anamnesis morbi

Arterial hypertension since 2000 with maximum BP 155/100 mm Hg.

Usual BP 120-130/70-80 mm Hg.

Multiple hospitalizations and treatment in outpatient clinic.

Previous hospitalization in CCH “UZ” in November 2013, after discharge ignored prescribed treatment.

Current hospitalization due to complaints described above.

Arterial hypertension since 1995 with maximum BP 155/105 mm Hg.

Usual BP 120/70 mm Hg.

Multiple hospitalizations and treatment in outpatient clinic.

Previous hospitalization in CCH “UZ” in January 2014, after discharge regularly took Arifon 2,5 mg in the morning.

Current hospitalization due to same complaints.

# Anamnesis vitae

**Appendectomy in young age.**

**Tuberculosis, diabetes mellitus, STD, viral hepatitis, rheumatism, psychiatric diseases in the anamnesis denies.**

**No pernicious habits.**

**No alcohol abuse.**

**Heredity is uncomplicated.**

**No allergic reactions in the past.**

**Right wrist joint fracture in 1983.**

**Tuberculosis, diabetes mellitus, STD, viral hepatitis, rheumatism, psychiatric diseases in the anamnesis denies.**

**No pernicious habits.**

**No alcohol abuse.**

**Heredity is uncomplicated.**

**No allergic reactions in the past.**

# Status presence objectivus

Patients overall condition is satisfactory, consciousness is clear, position is active.

Ectomorph body type.

Growth 175 cm, weight 68 kg, waist 90 cm, BMI 22,0 kg/m<sup>2</sup>.

Skin and visible mucous are pale-pink, clear.

Peripheral lymph nodes are not enlarged.

Thyroid gland can't be palpated.

Skeletal-muscular system without features.

Respiratory system: clear lung sound during percussion, vesicular breathing during auscultation without additional sounds.

CVS: heart rate is rhythmic, tones are muffled, accent of the S2 on aorta. HR = pulse = 65 bpm. BP 150/100 mm Hg.

Abdomen is normal in size, soft and painless during palpation.

Liver under the edge of ribs arch, painless.

No peripheral edema.

# Status presence objectivus

Patients overall condition is satisfactory, consciousness is clear, position is active.

Ectomorphic body type.

Growth 170 cm, weight 60 kg, waist 84 cm, BMI 21,0 kg/m<sup>2</sup>.

Skin and visible mucous are pale-pink, clear.

Peripheral lymph nodes are not enlarged.

Thyroid gland can't be palpated.

Skeletal-muscular system without features.

Respiratory system: clear lung sound during percussion, vesicular breathing during auscultation without additional sounds.

CVS: heart rate is rhythmic, tones are muffled, accent of the S2 on aorta. HR = pulse = 68 bpm. BP 150/90 mm Hg.

Abdomen is normal in size, soft and painless during palpation.

Liver under the edge of ribs arch, painless.

No peripheral edema.



# Investigation plan in the hospital

- **CBC**
- **Clinic urine analysis.**
- **Biochemical blood test (bilirubin, ALT, AST, glucose, creatinine, Na, K)**
- **Lipid profile**
- **Chest x-ray**
- **ECG**
- **Heart ultrasound with Doppler**
- **Kidneys ultrasound with Doppler**
- **Ophthalmologist consultation.**

# Investigation results

CBC			
<i>Indexes</i>	<i>Result (patient 1)</i>	<i>Result (patient 2)</i>	<i>Norm (SI units)</i>
<i>Hb</i>	<i>148 g/l</i>	<i>141 g/l</i>	<i>130-160 g/l</i>
<i>Erythrocytes</i>	<i>4,35 T/l</i>	<i>4,13 T/l</i>	<i>4-5 T/l</i>
<i>Platelet cell</i>	<i>283 g/l</i>	<i>235 g/l</i>	<i>180-320 g/L</i>
<i>Leucocytes</i>	<i>5,2 g/l</i>	<i>6,8 g/l</i>	<i>4-9 g/l</i>
<i>ESR</i>	<i>2 mm/h</i>	<i>4 mm/h</i>	<i>1-10 mm/h by Panchenkov</i>
<i>Neutrophils: myelocytes</i>	<i>-</i>	<i>-</i>	<i>-</i>
<i>band</i>	<i>1,0 %</i>	<i>-</i>	<i>1,0-6,0 %</i>
<i>segmented</i>	<i>66 %</i>	<i>3,0 %</i>	<i>47-72 %</i>
<i>Eosinophils</i>	<i>3 %</i>	<i>66 %</i>	<i>0,5-5,0 %</i>
<i>Basophils</i>	<i>-</i>		<i>0-1 %</i>
<i>Lymphocytes</i>	<i>21 %</i>	<i>1 %</i>	<i>19-37 %</i>
<i>Monocytes</i>	<i>9 %</i>	<i>-</i>	<i>3-11 %</i>
<i>Ht</i>	<i>41,5 %</i>	<i>26 %</i>	<i>40-48 %</i>

***Conclusion: indexes are in normal range.***

# Investigation results

<i>Urine test</i>			
<i>Indexes</i>	<i>Result (patient 1)</i>	<i>Result (patient 2)</i>	<i>Norm (SI units)</i>
<i>Volume</i>	<i>120,0 ml</i>	<i>110,0 ml</i>	<i>ml</i>
<i>Color</i>	<i>yellow</i>	<i>light- yellow</i>	<i>light- yellow</i>
<i>Feculence</i>	<i>weak</i>	<i>weak</i>	<i>weak</i>
<i>Density</i>	<i>1,020</i>	<i>1,017</i>	<i>1,015-1,025</i>
<i>pH</i>	<i>5,5</i>	<i>5,0</i>	<i>5,0-7,0</i>
<i>Protein</i>	<i>traces</i>	<i>-</i>	<i>traces</i>
<i>Glucose</i>	<i>-</i>	<i>-</i>	<i>-</i>
<i>Mucus</i>	<i>small amount</i>	<i>small amount</i>	<i>small amount</i>

*Conclusion: indexes are in normal range.*

# Investigation results

<i>Biochemical blood test</i>			
<i>Indexes</i>	<i>Result (patient 1)</i>	<i>Result (patient 2)</i>	<i>Norm (SI units)</i>
<i>Glucose</i>	<i>5,1</i>	<i>4,6</i>	<i>3,9-6,4 mmol/l</i>
<i>Creatinine</i>	<i>88,0</i>	<i>93,0</i>	<i>80-115 mkmol/l</i>
<i>Bilirubin: total</i>	<i>18,9</i>	<i>15,0</i>	<i>1,7-21 mkmol/l</i>
<i>conjugated</i>	<i>2,5</i>	<i>2,0</i>	<i>less 3,4 mkmol/l</i>
<i>unconjugated</i>	<i>16,4</i>	<i>13,4</i>	<i>less 17,6 mkmol/l</i>
<i>ALT</i>	<i>23</i>	<i>21</i>	<i>less 42 U/L</i>
<i>AST</i>	<i>20</i>	<i>27</i>	<i>less 35 U/L</i>
<i>Na</i>	<i>140</i>	<i>138</i>	<i>136-145 mmol/l</i>
<i>K</i>	<i>4,8</i>	<i>5,0</i>	<i>3.6-5.5 mmol/l</i>

*Conclusion: indexes are in normal range.*

# Investigation results

<i>Lipid profile</i>			
<i>Indexes</i>	<i>Result (patient 1)</i>	<i>Result (patient 2)</i>	<i>Norm (SI units)</i>
<i>Total cholesterol</i>	<i>2,97</i>	<i>4,0</i>	<i>до 5,2 mmol/l</i>
<i>VLDL</i>	<i>0,4635</i>	<i>0,349</i>	<i>до 1,0 mmol/l</i>
<i>LDL</i>	<i>1,4265</i>	<i>1,654</i>	<i>до 3,5 mmol/l</i>
<i>HDL</i>	<i>1,08</i>	<i>1,0</i>	<i>больше 0,9 mmol/l</i>
<i>Triglycerides</i>	<i>1,03</i>	<i>1,77</i>	<i>до 2,3 mmol/l</i>
<i>Atherogenic factor</i>	<i>1,75</i>	<i>3,0</i>	<i>до 3,0</i>

*Conclusion: indexes are in normal range.*

# Investigation results

**Chest x-ray:** Focal or infiltrative changes in lung are not detected. Roots are structured, not extended. Diaphragm is clearly outlined. Heart is slightly extended to the left. Aorta without features.

**ECG:** sinus rhythm, regular, HR 61 bpm. Hypertrophy of myocardium of left ventricle by wave's ratio criterion.

**Heart ultrasound with Doppler:** Hypertrophy of myocardium of left ventricle (LV posterior wall thickness: 12 mm, interventricular septum: 11,8 mm), systolic function is preserved (EF = 61%)

**Kidneys ultrasound with Doppler:** Incomplete doubling of left kidney, micro urolithiasis.

**Ophthalmologist consultation:** Angiopathy of retinal vessels of both eyes.

# Investigation results

Chest x-ray: Focal or infiltrative changes in lung are not detected. Roots are structured, not extended. Diaphragm is clearly outlined. Heart is slightly extended to the left. Aorta without features.

ECG: sinus rhythm, regular, HR 64 bpm. Hypertrophy of myocardium of left ventricle by wave's ratio criterion.

Heart ultrasound with Doppler: Hypertrophy of myocardium of left ventricle (LV posterior wall thickness: 12,3 mm, interventricular septum: 12,0 mm), systolic function is preserved (EF = 64%)

Kidneys ultrasound with Doppler: Micro urolithiasis.

Ophthalmologist consultation: Angiopathy of retinal vessels of both eyes.

# Diagnosis

**Classification of AH depends of the stage**  
*(recommendations of Ukrainian Heart Association, 2008)*

Stage	Degree of target organ damage
<i>I</i>	<i>Objective changes in the target organs are absent</i>
<i>II</i>	<b><i>Presence of objective evidence in target-organs without symptoms or dysfunctions:</i></b> <ul style="list-style-type: none"><li><i>• left ventricular hypertrophy (on ECG, ultrasound, Ro);</i></li><li><i>• generalized narrowing of the retinal arteries;</i></li><li><i>• microalbuminuria and/or increasing of creatinine concentration;</i></li><li><i>• carotid artery disease</i></li></ul>
<i>III</i>	<b><i>Presence of objective evidence in target-organs with symptoms or dysfunctions:</i></b> <ul style="list-style-type: none"><li><i>• heart: myocardial infarction, heart failure, II A - III stage;</i></li><li><i>• brain: stroke, transient ischemic attack, acute hypertensive encephalopathy, vascular dementia;</i></li><li><i>• eye-ground: hemorrhage and retinal exudates with/without papilledema of optic nerve;</i></li><li><i>• kidney: creatinine concentration in plasma &gt; 133 mmol/l</i></li></ul>



# Diagnosis

**Classification of AH depends of the degree**  
*(ESH/ESC Guidelines for the management of arterial hypertension, 2013)*

<b>Category</b>	<b>Systolic blood pressure (mm Hg)</b>	<b>Diastolic blood pressure (mm Hg)</b>
<b><i>Optimal blood pressure</i></b>	<b><i>&lt; 120</i></b>	<b><i>&lt; 80</i></b>
<b><i>Normal blood pressure</i></b>	<b><i>&lt; 130</i></b>	<b><i>&lt; 85</i></b>
<b><i>Normal blood pressure</i></b>	<b><i>&lt; 130</i></b>	<b><i>&lt; 85</i></b>
<b><i>Mild hypertension (1 degree)</i></b>	<b><i>140-159</i></b>	<b><i>90-99</i></b>
<b><i>Moderate hypertension (2 degree)</i></b>	<b><i>160-179</i></b>	<b><i>100-109</i></b>
<b><i>Severe hypertension (3 degree)</i></b>	<b><i>&gt; 180</i></b>	<b><i>&gt; 100</i></b>
<b><i>Isolation systolic hypertension</i></b>	<b><i>&gt; 140</i></b>	<b><i>&gt; 90</i></b>

# Diagnosis

## Risk stratification

*(ESH/ESC Guidelines for the management of arterial hypertension, 2013)*

Blood pressure (mmHg)					
Other risk factors, OD or Disease	Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP $\geq 180$ or DBP $\geq 110$
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1–2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors, MS, OD or Diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

# Clinical diagnosis

Arterial hypertension II stage 1 degree, HF 0 stage,  
moderate additional risk

Arterial hypertension II stage 1 degree, HF 0 stage,  
moderate additional risk

# Treatment

**Lifestyle modification: control of body weight, diet, regular exercises.**

**Drugs therapy: perindopril 5 mg 1 time per day in the evening, aspirin-cardio 100 mg in the evening.**

**Non-drug therapy:**

**for patient 1 – 10 biofeedback sessions in the loop of paced breathing under the control of heart rate variability parameters;**

**for patient 2 – 10 biofeedback pseudosessions under the control of heart rate variability parameters.**

# Methods of research

## Devices:

- computer diagnostic complex "CardioLab 2009" ("KhAI-Medica");
- module "Biofeedback" (programmatically connected aural-visual breathing metronome and algorithm of HRV parameters estimation).





# Methods of research

Efficacy of biofeedback was evaluated by comparing the values of:

- systolic, diastolic and pulse blood pressure (SBP, DBP and PP, respectively);
- BQI integral index – parameter that reflects all qualitative changes of biofeedback process:
  - optimality (O) – estimation of farness of regulatory systems from optimal state during whole period of session;
  - sensitivity (S) – estimation of receptivity of regulatory systems to paced breathing;
  - effectiveness (E) – estimation of approaching range of HRV parameters to optimal physiological state during execution of optimal bioreverse control algorithm.

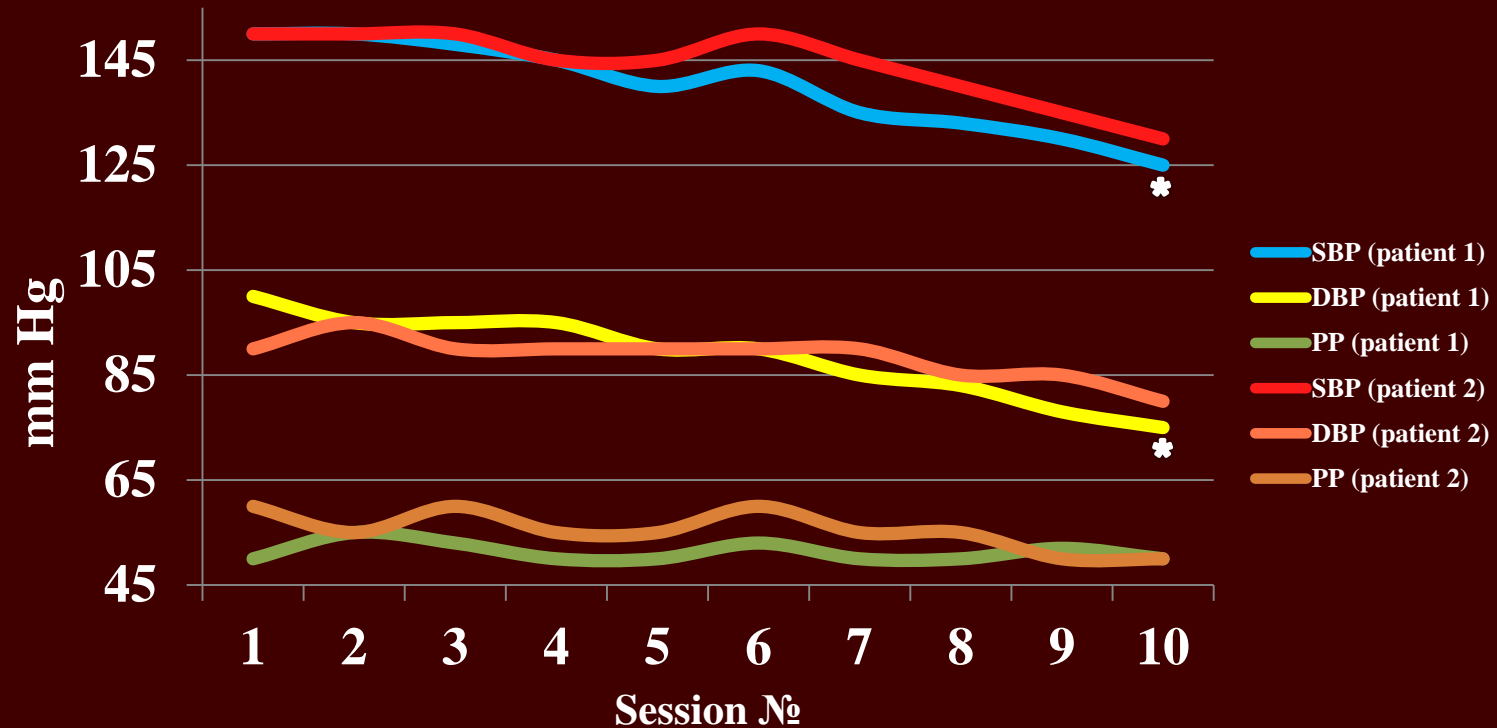
*Statistical analysis of the results for each subject was carried out using Microsoft Excel computer software.*

*The significance of differences between groups on the stages of the study was determined using the U-Mann-Whitney test.*

*The significance of differences between the values of the indices at given stage and before treatment was determined using the T-Wilcoxon test.*

# Results

## *Dynamics of SBP, DBP and PP during 10 days of stationary treatment in both patients*

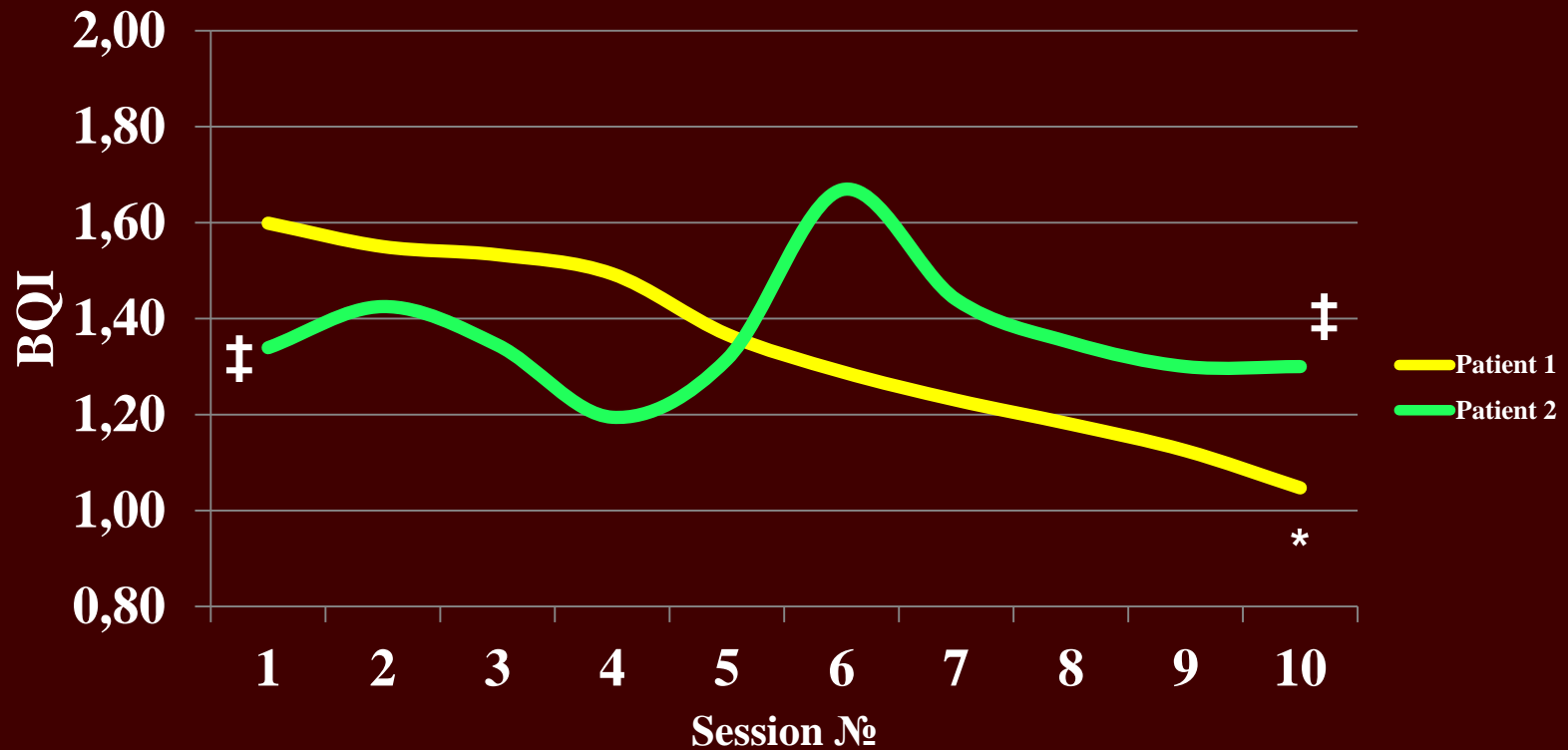


*Notes: \* -  $P < 0.05$  at the sessions against initial values; ‡ -  $P < 0.05$  between patients at the current session.*

*During the same treatment in both patients systemic biofeedback implementation contributed to lower values aforementioned indices.*

# Results

## *BQI index dynamics in both patients during 10 sessions*



**Notes:** \* -  $P < 0.05$  at the sessions against initial values; ‡ -  $P < 0.05$  between patients at the current session.

**Systematic biofeedback sessions in patient 1 contributed natural approximation of regulation to the optimal level, whereas in patient 2 it index fluctuated within suboptimal level without reaching the target level.**



# Conclusions

- *Biofeedback in a closed loop of heart rate variability and paced breathing allow to optimize the regulatory systems condition of the body in patients with arterial hypertension.*
- *Combination of biofeedback sessions and drug treatment is significantly superior in effectiveness of the isolated pharmacological therapy.*
- *The effectiveness of biofeedback in a closed loop of heart rate variability and paced breathing allows us to recommend it as a component of complex therapy for patients with arterial hypertension.*

